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SEP 2 9 2005

#### SHARCHING AUTHORITY

From the INTERNATIONAL SHARCHING ACTHORITY	(			
To: JANE MASSEY LICATA	PCT			
LICATA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053	NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION			
	(PCT Rule 44.1)			
	Date of mailing (day/month/year)			
Applicant's or agent's file reference ISPH-0852	FOR FURTHER ACTION See paragraphs 1 and 4 below			
International application No. PCT/US04/13379	International filing date (day/month/year) 30 April 2004 (30.04.2004)			
Applicant ISIS PHARMAÇEUTICALS, INC.				
IND TITEMANACEDITORIO, INC.				
1. The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.				
Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the clai	ms of the international application (see Rule 46):			
	normally two months from the date of transmittal of the international			
Where? Directly to the International Eureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Fuesimile No.: (41-22) 338.82.70.				
For more detailed instructions, see the notes on the accompanying sheet.				
2. The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.				
3. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that				
the protest together with the decision thereon has been transmitted to the International Eureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.				
no decision has been made yet on the protest; the ap	<del>-</del>			
4. Reminders				
Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Burean. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.				
The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.				
Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.				
In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.				
See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the PCT Applicant's Guide,				
Volume II, National Chapters and the WIPO Internet site.				
Name and mailing address of the ISA/ US	Authorized officer and and			
Mail Stop PCT, Attn: ISA/US	Jane Zara			
Commissioner for Patents P.O. Bux 1450	1 1 70000			
Alexandria; Virginia 22313-1450 Facsimile No. (703) 305-3230	Telephone No. (57/)222-/600			
Form PCT/ISA/220 (January 2004)  (See notes on accompanying th				

ISIS DOCKETING Action to be taken: Due Date(s): PCM Entry by:

counsel

### PATENT COOPERATION TREATY

# **PCT**

#### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference JSPH-0852	FOR FURTHER  see Form PCT/ISA/220  ACTION  as well as, where applicable, iron 5 below.				
International application No. PCT/US04/13379	International filing date (day/month/year) 30 April 2004 (30.04.2004)	(Earliest) Priority Date (day/month/year) 04 June 2003 (04.06.2003)			
Applicant ISIS PHARMACEUTICALS, INC.					
This international search report has been prepared by this International Scarching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.  This international search report consists of a total of sheets.  It is also accompanied by a copy of each prior srt document cited in this report.  Basis of the Report  a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed.  a translation of the international application into					
5. With regard to the abstract, the text is approved as sub					
the text has been establishe may, within one month from	ed, according to Rule 38.2(b), by this Authorit in the date of mailing of this international scan	ty as it appears in Box No. IV. The applicant report, submit comments to this Authority.			
as suggested by the as selected by this	e published with the abstract is Figure No c applicant.  Authority, because the applicant failed to sug  Authority, because this figure better character  published with the abstract.	gest a figure.			

Form PCT/ISA/210 (first sheet) (April 2005)

## INTERNATIONAL SEARCH REPORT

International condi-

Box No.	I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)
1. With reinvent	egard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed non, the international search was carried out on the basis of type of material
	a sequence listing  Table(s) related to the sequence listing
,	format of material
Ъ.	on beher
	in electronic form
c,	time of filing/furnishing  contained in the international application as filed
	filed together with the international application in electronic form
	furnished subsequently to this Authority for the purposes of search
2.	In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3.	Additional comments:
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## INTERNATIONAL SEARCH REPORT

PCT/US04/13379

A CLAS	A CLASSIFICATION OF SUBJECT MATTER				
ĬPC(7)	: C12Q 1/68; C12P 19/34; C12N 15/63, 15/88; C0 : 435/6, 91.1, 91.31, 455; 536/23.1, 24.5; 514/44	7H 21/02, 21/04; AUIN 43/04			
US CL According to	International Patent Classification (IPC) or to both net	onal clussification and IPC			
B. FIELL	OS SEARCHED				
Minimum doc	cumentation searched (classification system followed b	y classification symbols)			
	5/6, 91.1, 91.31, 455; 536/23.1, 24.5; 514/44		İ		
Documentatio	on searched other than minimum documentation to the	extent that such documents are included in	the fields searched		
Electronic de	ta base consulted during the international search (name	of duta base and, where practicable, search	h terms used)		
	, Sequence Search	•	-		
C. DOCT	UMENTS CONSIDERED TO BE RELEVANT				
Category *	Citation of document, with indication, where ap	propriate, of the relevant passages	Relevant to claim No.		
		45 500 1: 110 15 15 01	1-18		
Y	US 6,506,559 (FIRE et al) 14 January 2003, abstract	, 4-5, 7-8-9, Claims 1-10, 12, 13, 21.	1-16		
Y	Y US 6,096,722 (BENNETT et al) 1 August 2000 (col. 2, 6, 8, 11-12, 17, 20, 24-25, 37-39,		1-18		
	43-48, 54-55, claims 1, 2, 6, 7, 8-22).	·			
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l					
Fronther	r documents are listed in the continuation of Box C.	See patent family annex.			
	Special cubgaries of cited documents;	"T" later document published after the interna-	nional filing data or priority data		
	•	and not in conflict with the application be principle or theory underlying the inventi-	it cited to understand the		
	t defining the general state of the ar which is not considered to be of relevance				
"B" earlier ap	plication or patent published on or after the international filing date	"X" document of particular relevance; the claim	med invention camiot be to involve on inventive step		
"L" document	r which may throw doubts on priority claim(s) or which is cited to	when the document is taken alone			
daildarze	the publication date of mother citation or other special reason (as	"Y" document of particular relevance; the clai considered to involve an inventive step w			
specified	·	with one or more other such documents, e			
"O" document	t referring to an oral disclosure, use, exhibition or other messas	to a penson, skilled in the art			
	t published prior to the invernational filing date but later than the ate claimed	"&" device , reamber of the same patent fan	nily		
Date of the a	ctual completion of the international search	Date of mailing of the international search	h report		
13 Septembe	<del>a</del> 2005 (13.09,2005)	27 SEP 2005			
	miling address of the ISA/US	Authorized officer	02		
	il Stop PCT, Atm: ISA/US	Jane Zara	7		
P.C	mmissioner for Patents D. Box 1450				
	P.O. Box 1450 Alexandria, Virginia 22313-1450 Telephone No. (53) 9232-1400 (60)				